IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application: Glover et al.

Serial No.: To be Assigned Examiner: E. Crane

Filing Date: To be Assigned Art Unit: 1623

For: NOVEL CRYSTALLINE FORMS OF AN ANTIVIRAL BENZIMIDAZOLE COMPOUND

Commissioner for Patents
Washington D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to the first Office Action, please amend and reconsider the instant application in view of the following amendments and remarks.

In the Specification:

At page 1, line 1, please insert the following new paragraph:

--Cross-References to Related Applications

This application is a continuation of U.S. Patent Application Serial No. 09/647,962, filed 6 October 2000, which is a Rule 371 Application of PCT/EP99/02214, filed 1 April 1999, which claims priority to Great Britain Patent Application No. 9807354.7, filed 7 April 1998.--

In the Claims:

Please cancel claims 1-10, 12, 13 and 15. Please amend claims 11 and 14 as follows. Please add new claims 16-21. The following clean claims reflect the amendments being made herein. A marked-up copy of the amended claims is attached hereto.

11. (Amended) A pharmaceutical composition comprising a crystalline form of Form II 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 2**, wherein

said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation, and at least one pharmaceutically acceptable carrier therefor.

14. (Amended) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of Form II 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 2**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation.

16. (New) A pharmaceutical composition comprising a crystalline form of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 3**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation, and at least one pharmaceutically acceptable carrier therefor.

17. (New) A pharmaceutical composition comprising a crystalline form of Form V 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 5**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation, and at least one pharmaceutically acceptable carrier therefor.

18. (New) A pharmaceutical composition comprising an admixture of two or more forms or solvates of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole selected from the group consisting of Form I, Form II, ethanol solvate, Form IV, Form V, and amorphous, and at least one pharmaceutically acceptable carrier therefor.

19. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 3**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation,.

20. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of Form V 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 5**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation.

21. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a composition comprising an admixture of two or more crystalline forms or solvates of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole selected from the group consisting of Form I, Form II, ethanol solvate, Form IV, Form V, and amorphous.

Remarks

Currently Claims 11, 14 and 16-21 are pending. Claims 1-10 and 15 have been canceled, as they are allowed in parent patent application serial number 09/647,962. Claims 11 and 14 have been amended to place the claims in independent form. New claims 16-21 are added to complete the record. Support for these claims can be found in Applicants original specification including the claims as filed. An abstract on a separate page is provided herewith.

Claims 11 and 14 were rejected in the parent application under the judicially created doctrine of obviousness-type double patenting, the Office Action stating that the claims were unpatentable over claims 1-30 of U.S. Patent No. 6,077,832 ('832 patent). The Examiner indicated that the claims read on pharmaceutical compositions and methods of treatment wherein the crystallinity of the active ingredient has no bearing on the pharmacological or medicinal activity of the composition.

Applicants respectfully submit that the instantly claimed invention represents an improvement over the invention claimed in the '832 patent that is encompassed by the claims of the '832 patent. Applicants submit that the crystalline forms of the compound have the same pharmaceutical activity and uses as disclosed for the amorphous compound in the '832 patent. However, the presently claimed invention is restricted to compositions and methods which include specifically claimed crystalline forms which are neither disclosed nor suggested by the '832 claims.

Applicants acknowledge that in certain pharmaceutical compositions, such as solutions where the compound is completely solubilized, the specific crystal form of the compound would be indistinguishable. However, in other pharmaceutical compositions, e.g., solid dosage formulations, the crystal form of the compound would indeed be determinable and distinct from formulations containing the amorphous compound of the '832 patent. The instantly pending composition claims are restricted to compositions containing the specified crystalline forms of the compound. Hence the claim does not read on pharmaceutical compositions wherein the compound does not exist in crystalline form. Similarly, the instantly pending method claims are also restricted to methods of treatment which comprise administering the compound in crystalline form and do not read on methods of treatment which do not involve administering the compound in crystalline form.

Applicants respectfully submit that the instant application is in condition for substantive examination, which action is respectfully requested. The Examiner is invited to contact the undersigned at 483-8222, to discuss this case further if desired.

Respectfully submitted,

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Marked-Up Copy of Amended Claims

11. (Amended) A pharmaceutical composition comprising [a compound as claimed in any one of claims 1 to 6] a crystalline form of Form II 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 2**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation, and at least one pharmaceutically acceptable carrier therefor.

14. (Amended) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of Form II 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 2**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation [a solvate or crystalline form of 5,6,-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole as claimed in any one of claims 1 to 6].

16. (New) A pharmaceutical composition comprising a crystalline form of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 3**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation, and at least one pharmaceutically acceptable carrier therefor.

17. (New) A pharmaceutical composition comprising a crystalline form of Form V 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 5**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation,

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and at least one pharmaceutically acceptable carrier therefor.

18. (New) A pharmaceutical composition comprising an admixture of two or more forms or solvates of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole selected from the group consisting of Form I, Form II, ethanol solvate, Form IV, Form V, and amorphous, and at least one pharmaceutically acceptable carrier therefor.

19. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 3**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation,.

20. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a crystalline form of Form V 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole having substantially the same X-ray powder diffraction pattern as **Figure 5**, wherein said X-ray powder diffraction pattern is obtained with a diffractometer equipped with a diffracted beam curved graphite monochromator using copper Kα X-radiation.

21. (New) A method for the treatment of a herpes viral infection in a human which comprises administering to the human host, an effective antiviral amount of a composition comprising an admixture of two or more crystalline forms or solvates of 5,6-dichloro-2-(isopropylamino)-1-β-L-ribofuranosyl-1H-benzimidazole selected from the group consisting of Form I, Form II, ethanol solvate, Form IV, Form V, and amorphous.